

**UNITED STATES DISTRICT COURT  
EASTERN DISTRICT OF MISSOURI  
SOUTHEASTERN DIVISION**

**JUDITH PARMENTIER, Personal  
Representative of the Estate of  
Linda Johnson,**

**Plaintiff,**

**vs.**

**NOVARTIS PHARMACEUTICALS  
CORPORATION,**

**Defendant.**

**Case No. 1:12-CV-45 SNLJ**

**MEMORANDUM AND ORDER**

Plaintiff Judith Parmentier alleges that her sister, Linda Johnson, developed osteonecrosis of the jaw (“ONJ”) as a result of infusions of Zometa and/or Aredia, which are drugs used in cancer treatment and which are manufactured by defendant Novartis Pharmaceuticals Corporation (“Novartis”). This matter is before the Court on defendant’s Motion to Exclude Causation Testimony of Plaintiff’s Experts (#71).

**I. Factual Background<sup>1</sup>**

Zometa and Aredia are “bisphosphonate drugs” prescribed to cancer patients for the purpose of reducing or delaying bone fractures or spinal cord pressure that can result from bone damage from certain cancers. Specifically, the Food and Drug Administration (“FDA”) approved Aredia on October 31, 1991 for treatment of hypercalcemia of malignancy and in September 1995 for other indications. The FDA approved Zometa in 2001 for treatment of

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<sup>1</sup>Some factual background is taken from the parties’ briefing on defendant’s Motion for Summary Judgment (#73).

hypercalcemia of malignancy.

Osteonecrosis of the jaw — a painful condition in which the jawbone dies — has been reported in scientific literature since the 19th century. The parties dispute when the connection between bisphosphonate drugs and ONJ was made. Defendant states that it received its first report regarding development of ONJ in a patient receiving bisphosphonates in December 2002; plaintiff maintains that ONJ was reported during clinical trials dating back to 1992 and that phosphorus necrosis of the jaw was known in the 19th century. In 2003, Novartis voluntarily revised the product labeling for Aredia and Zometa to include information about ONJ. Plaintiff disputes that the labeling changes accurately reflected the information Novartis had received, and plaintiff states that Novartis added false information to the Aredia label.

Linda Johnson was diagnosed with breast cancer in 1992 and with metastatic breast cancer in 2001. Ms. Johnson's oncologist, Dr. Ray Peters, prescribed Zometa in 2001 to prevent skeletal related problems. In 2002, Ms. Johnson had two teeth extracted. In 2004, Ms. Johnson visited an oral surgeon, Dr. Randal Begley, with complaints that her jaw had not healed since those extractions. Also in 2004, Dr. Peters switched Ms. Johnson from Zometa to Aredia. In 2005, Ms. Johnson was diagnosed with "osteonecrosis of the mandible on a clinical basis." She alleges in this lawsuit that Aredia and Zometa caused her ONJ.<sup>2</sup>

## **II. Procedural Background**

This case was originally filed in the Southern District of New York in January 2006. Because numerous other plaintiffs filed similar lawsuits against Novartis in federal courts across

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<sup>2</sup>Ms. Johnson died in May 2007. Her sister, Judith Parmienter, personal representative for Ms. Johnson's estate, was substituted as plaintiff.

the country, the Judicial Panel on Multidistrict Litigation consolidated those cases for pretrial management in the Middle District of Tennessee in *In re: Aredia and Zometa Products Liability Litigation*, 3:06-md-1760 (“MDL 1760” or simply, the “MDL”). Plaintiff’s case joined MDL 1760 in May 2006.

The MDL comprises hundreds of cases, and the filings in the MDL number several thousand. The MDL Court ruled on a number of pretrial matters relevant to the instant litigation, which will be discussed below. On October 4, 2011, this matter was remanded back to the Southern District of New York. Then, because the fact witnesses and plaintiff all resided in or around this District, the parties voluntarily transferred the case to the Eastern District of Missouri, Southeastern Division, on March 13, 2012.

As stated above, this case joined the MDL in May 2006. Defendant filed its Motion for Summary Judgment Based on Failure of General Causation Proof Under *Daubert* on June 1, 2009 (MDL Document No. 2374). The MDL Court denied the motion on August 13, 2009 (MDL Document No. 2764), holding that genuine issues of fact existed as to whether plaintiffs could prove general causation, that is, whether or not defendant’s drugs Aredia and Zometa can cause ONJ in its users. That Court also declined to exclude plaintiff’s general causation experts from testifying.

At the time of transfer to this District, three motions were pending: (1) Defendant’s Motion to Exclude Testimony of Plaintiffs’ Experts Fletcher, Skubitz, Vogel, Ray, Parisian, and Marx (#70), (2) Defendant’s Motion to Exclude Testimony of Plaintiff’s Causation Experts<sup>3</sup>

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<sup>3</sup>Defendant seeks to exclude plaintiff’s retained causation expert (Dr. Ramin Shabtaie) and plaintiff’s non-retained experts (Drs. Ray Peters and Randal Begley).

(#71), and (3) Defendant's Motion for Summary Judgment (#73). The motions have been fully briefed and are ripe for adjudication. This memorandum and order addresses only defendant's Motion to Exclude Testimony of Plaintiff's Causation Experts (#71).

### **III. Discussion**

In order to prevail on any of her claims, plaintiff must prove that Zometa and Aredia caused Ms. Johnson's injuries. *See Chism v. W.R. Grace & Co.*, 158 F.3d 988, 991 (8th Cir. 1988) (applying Missouri law). This requires plaintiff to prove both that the drugs can cause ONJ in general (general causation) and that the drugs did so in Ms. Johnson (specific causation). Because this case involves a "sophisticated" injury involving scientific techniques for diagnosis, expert testimony is required to prove causation. *Turner v. Iowa Fire Equip. Co.*, 229 F.3d 1202, 1210 (8th Cir. 2000); *Wright v. Barr*, 62 S.W.3d 509, 524 (Mo. Ct. App. 2001). "When the plaintiff relies on expert testimony to provide evidence as to causation when there are two or more possible causes, that testimony must be given to a reasonable degree of medical certainty." *Wright*, 62 S.W.3d at 524; *see also Turner*, 229 F.3d at 1209.

This Court must act as a "gatekeeper" to "insure that proffered expert testimony is both relevant and reliable." *Wagner v. Hesston Corp.*, 450 F.3d 756, 758 (8th Cir. 2006) (quoting *Anderson v. Raymond Corp.*, 340 F.3d 520, 523 (8th Cir. 2003)); *see also Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 589 (1993). Federal Rule of Evidence 702 governs the standard for this Court's admission of expert testimony. It provides:

A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if: (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles

and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702.

Here, plaintiffs have identified three experts through whom they plan to prove specific causation, *i.e.*, that defendant's drugs did in fact cause Ms. Johnson's ONJ: (1) retained expert Dr. Ramin Shabtaie, (2) non-retained expert Dr. Randal Begley, and (3) non-retained expert Dr. Ray Peters.

**A. Dr. Ramin Shabtaie**

Dr. Shabtaie is an oral and maxillofacial surgeon, licensed in California, who has been practicing for 11 years. He is both in private practice and a part-time attending physician and Clinical Instructor with the UCLA Oral and Maxillofacial Department. He is also a part-time clinical instructor at Cedars-Sinai Medical Center and at the UCLA School of Dentistry, Department of Oral and Maxillofacial Surgery. He first became aware of bisphosphonate related ONJ ("BRONJ") in early 2004. He keeps a file of medical literature relating to bisphosphonate induced ONJ; he gives lectures that discuss ONJ and bisphosphonate-related ONJ; and he has written an article about bisphosphonates and ONJ that was published by the Western Los Angeles Dental Society. Over the past six years, he has been involved in the treatment of six patients who have had ONJ. On the other hand, Dr. Shabtaie is not board certified in oral and maxillofacial surgery or in any other field of medicine or dentistry, and plaintiff's counsel admitted that Dr. Shabtaie was not an expert in general causation with respect to bisphosphonates and ONJ in another MDL case, *Carter v. Novartis Pharmaceutical Corp.*, No. 3:6-cv-386 (M.D. Tenn.).

In this case, Dr. Shabtaie testified that he concluded, to a reasonable degree of medical certainty, that Ms. Johnson developed ONJ as a result of being treated with Zometa, and perhaps Aredia as well. Dr. Shabtaie never treated or examined Ms. Johnson. Rather, he reviewed Ms. Johnson's medical records and the deposition transcripts of Drs. Begley and Bell. He also states that he relied on his experience as an oral surgeon, his experience evaluating patients with BRONJ, available medical literature on BRONJ, his knowledge of bone biology, and information he learned through collaboration with his colleagues. Plaintiff contends that Dr. Shabtaie performed a "differential diagnosis" to rule out other potential causes of ONJ.

However, Dr. Shabtaie stated at his depositions that he is *not an expert* at diagnosing the causes of ONJ. When asked "do you consider yourself an expert in diagnosing the cause of osteonecrosis of the jaw?", he responded, "I'm qualified to diagnose. I wouldn't call myself an expert." At a subsequent deposition, Dr. Shabtaie stated, "At that point, the question was do I consider myself an expert in diagnosing the cause of osteonecrosis of the jaw? I'm not a researcher and I haven't spent as much time as some others in distinguishing the causes of osteonecrosis, *so I'm not an expert in diagnosing the causes of osteonecrosis*. Again, I base my opinions on what's available to me." (Emphasis added.)

Defendant argues that Dr. Shabtaie's admission that he is not an expert at diagnosing the causes of ONJ precludes him from testifying as an expert on specific causation. This Court agrees. Diagnosing a condition is quite different from determining causation. *See Turner*, 229 F.3d at 1208 (discussing the difference between diagnosis of a condition and determining its cause). Plaintiff does nothing to refute defendant's argument, and the only time she addresses Shabtaie's disclaimer is in response to the defendant's statement of undisputed facts (#78-1).

She states that “[t]he designated testimony is taken out of context.” Dr. Shabtaie, however, provides the context for his statement, and he unequivocally states that he does not consider himself to be an expert on causation. “If an expert is not qualified to opine in a particular area, . . . such testimony is excluded under *Daubert*.” *In re Baycol Prods. Lit.*, 532 F. Supp. 2d 1029, 1047 (D. Minn. 2007) (excluding testimony where expert admitted he was not qualified to provide an expert opinion).

The MDL Court addressed a similar problem with another plaintiff’s causation expert in *In re Aredia and Zometa Prods. Liability Lit.*, No. 3:6-md-1760, 2010 WL 4970923 (M.D. Tenn. Dec. 7, 2010). There, a dentist who was intended to provide specific causation testimony “testified that he did not consider himself to be an expert” in bisphosphonates or in ONJ generally. *Id.* at \*1. Further, his opinion was based on literature and information given to him by the plaintiff’s attorneys, and he did not rule out other potential causes of the patient’s ONJ. The court found that the dentist “is not qualified to testify about the specific cause of [the patient’s] ONJ in this case. His opinion lacks the sound methodology and foundation required under the standards of *Daubert*, and he has not demonstrated the ‘extensive familiarity with the subject’ to support its reliability.” *Id.* at \*4.

Similarly, here, even if Dr. Shabtaie had not disclaimed his qualification as an expert, his testimony would be excludable under *Daubert* due to his inadequate methodology and foundation. Dr. Shabtaie claims he performed a “differential diagnosis” to conclude that Zometa, and possibly Aredia, caused Ms. Johnson’s ONJ. In the Eighth Circuit, “a medical opinion about causation, based upon a proper differential diagnosis, is sufficiently reliable to satisfy *Daubert*.” *Turner*, 229 F.3d at 1208. A differential diagnosis is performed as follows:

[A] physician begins by “ruling in” all scientifically plausible causes of the plaintiff’s injury. The physician then “rules out” the least plausible causes of injury until the most likely cause remains. The final result of a differential diagnosis is the expert’s conclusion that a defendant’s product caused (or did not cause) the plaintiff’s injury.

*Glastetter v. Novartis Pharmaceuticals Corp.*, 252 F.3d 986, 989 (8th Cir. 2001). Here, Dr.

Shabtaie states that he considered and ruled out (1) radiation therapy, (2) corticosteroids, (3) jaw metastasis, and (4) osteomyelitis as possible causes of Ms. Johnson’s ONJ. However, Dr.

Shabtaie failed to rule out several known causes of ONJ: although Dr. Shabtaie testified that both “severe alcoholism” and the effects of smoking could mimic osteonecrosis of the jaw, he was unaware that Ms. Johnson had been hospitalized for alcoholism, and he believed that Ms. Johnson had reduced her tobacco use, when in fact she had increased her smoking to three packs a day in 2003. When asked whether he had ruled out smoking as a cause or contributing factor to Ms. Johnson’s ONJ, Dr. Shabtaie answered, “it could have been a contributing factor.”

Moreover, Dr. Shabtaie acknowledged in his affidavit that radiation therapy precludes a diagnosis of bisphosphonate-related ONJ, and he stated that he had ruled out Ms. Johnson’s radiation therapy to the “throat” as a cause of her ONJ “based on her available medical records.” But at his deposition, he admitted that had not reviewed records of the radiation therapy to her neck that took place in 1992. Further, Dr. Shabtaie says he ruled out radiation as a cause of ONJ because her medical records do not “mention...mucositis or xerostomia,” but he did not review dental records between the time of her 1993 radiation therapy and 2004 (two years after Ms. Johnson’s tooth extractions failed to heal).

In addition, Dr. Shabtaie’s basis for ruling out osteomyelitis was that Ms. Johnson’s records did not reflect “discharge, swelling, [or] pus coming out of the area.” However, both Dr.



Peters and Dr. Begley (Ms. Johnson's treating physician and oral surgeon) had diagnosed Ms. Johnson with osteomyelitis.

Finally, Dr. Shabtaie's exclusion of metastasis is also flawed because he testified that in "2001, 2002, ...there's no real record of the jaw being involved as far as metastatic activity," while at the same time recognizing the "studies down the road that show[] that there's some activities in the jaw," such as the 2003 MRI mentioned in his affidavit. Shabtaie freely admits that "metastasis could have been caused in her case."

Dr. Shabtaie's methodology was flawed. He did not rule out possible causes of Ms. Johnson's ONJ because he did not have sufficient information to do so (*e.g.*, he was unaware of Ms. Johnson's alcoholism and three-pack-a-day smoking habit; he did not review her radiation treatment records; and he did not review pertinent dental records). He dismisses the possibility that her ONJ was caused by something other than bisphosphonates despite the contrary diagnoses of other physicians, and despite not having reviewed all of Ms. Johnson's relevant medical and dental records. Dr. Shabtaie's methodology lacks the reliable foundation required under Rule 702 and *Daubert*, and, as a result, Dr. Shabtaie's specific causation testimony will be excluded.

**B. Dr. Randal Begley and Dr. Ray Peters**

Dr. Begley was one of Ms. Johnson's treating oral surgeons. Dr. Peters, who was Ms. Johnson's oncologist, referred her to Dr. Begley in January 2004 for treatment of exposed bone in her lower jaw. Dr. Begley testified that he did not diagnose Ms. Johnson's jaw problems as being bisphosphonate-related while he was treating her because he had never heard of the association. He did not learn about BRONJ until after she stopped seeing him.

Dr. Begley was not able to state his opinion to a reasonable degree of medical certainty

that bisphosphonates had caused Ms. Johnson's jaw problems. Dr. Begley was asked, "do you have an opinion to a reasonable degree of medical certainty as to what condition Ms. Johnson had in her lower mandible when you treated her?" Dr. Begley responded, "...I would say that the bisphosphonate had something to do with the bone not healing, but . . . I cannot rule out that, that a metastasis was not in that area, too, according to the PET scan lighting up like her other areas of her metastasis. So without the biopsy report, you know, I can't say that they both weren't going on." Plaintiff appears to believe Dr. Begley provides admissible expert testimony on causation "based on what he has learned (both from treating other patients and continuing education)," but because Dr. Begley himself testified that he could not rule out metastasis, this Court cannot allow his testimony.

Dr. Peters was Ms. Johnson's treating oncologist. At his deposition, he stated "I did not review [the literature] at any length . . . . I am coming in here to testify to the facts. I'm not here to give an opinion." When asked "you can't testify to a reasonable degree of medical certainty that a metastatic lesion to her mandible was ruled out. Is that correct?", Dr. Peters answered "That's correct." Dr. Peters, then, disclaims that he is providing expert testimony on causation, and he testified that he did not rule out metastasis.

Plaintiff suggests that because defendant has identified Drs. Peters and Begley as potential sources of expert testimony, defendant has forfeited any argument in favor of excluding their testimony. However, defendant's challenge is to their causation testimony, not to their testimony regarding other matters. The MDL Court addressed specific causation testimony of other treating physicians as follows:

As this Court has previously held, generally a treating physician may provide

expert testimony regarding a patient's illness, the appropriate diagnosis for that illness, and the cause of the illness. However, a treating physician's testimony remains subject to the requirement set forth in *Daubert*, that an expert's opinion testimony must have a reliable basis in the knowledge and experience of his discipline. A medical doctor is generally competent to testify regarding matters within his or her own professional experience. When, however, the doctor strays from such professional knowledge, his or her testimony becomes less reliable and more likely to be excluded under Rule 702.

*In re Aredia and Zometa Products Liability Litigation*, 754 F. Supp. 2d 934, 936 (M.D. Tenn. 2010) (internal citations and footnote omitted). In the Eighth Circuit as well, treating physicians such as Peters and Begley are "subject to the same standards of scientific reliability that govern the expert opinions of physicians hired solely for purposes of litigation." *Turner*, 229 F.3d at 1207. Here, Dr. Peters disclaims that he is testifying as an expert, and there appears to be no evidence supporting Dr. Begley's status as an expert in diagnosing the cause of ONJ. Additionally, it appears that neither Dr. Peters nor Dr. Begley even tried to perform a differential diagnosis on Ms. Johnson to determine what caused her ONJ. Neither can state to a reasonable degree of medical certainty what caused Ms. Johnson's ONJ, and neither may provide specific causation testimony to support plaintiff's claims.


#### IV. CONCLUSION

Plaintiff's three proposed specific causation experts do not satisfy the standards of *Daubert* and Rule 702. As a result, the Court will exclude their testimony regarding specific causation of Ms. Johnson's ONJ.

Accordingly,

**IT IS HEREBY ORDERED** that Defendant's Motion to Exclude Testimony of Plaintiff's Causation Experts (#71) is GRANTED.

Dated this 19th day of June, 2012.

  
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STEPHEN N. LIMBAUGH, JR  
UNITED STATES DISTRICT JUDGE